Fetal Outcomes of Prenatally Diagnosed Congenital Diaphragmatic Hernia: Nine Years of Clinical Experience in a Canadian Tertiary Hospital

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Abstract

Objective: To summarize the clinical outcome of congenital diaphragmatic hernia (CDH) identified on prenatal ultrasound.

Method: We reviewed prenatally detected cases of CDH diagnosed between July 2000 and September 2009 at a single tertiary-care facility.

Results: Ninety-one cases were identified. Sixty-nine cases had complete medical records including karyotype. Of these, 40 were isolated defects and 29 cases had additional congenital or chromosome anomalies. An abnormal karyotype was present in 17.4% overall, affecting 2.5% of cases of isolated CDH (1/40) and 37.9% of cases of non-isolated CDH (11/29). The rate of termination of pregnancy in cases of isolated CDH diagnosed prior to 24 weeks was 33.3% (10/30), and in cases of non-isolated CDH it was 73.9% (17/23). The survival rate of the 44 liveborn infants was 66.7% (24/36) for those with isolated CDH and 37.5% (3/8) for those with non-isolated CDH. The decision to terminate the pregnancy was made in 73.9% of fetuses with prenatally diagnosed karyotype or additional anatomical abnormalities, in contrast to 37.5% of prenatally diagnosed isolated CDH.

Conclusion: The outcomes of pregnancies that continue after identification of CDH are in keeping with previous reports, with an overall survival rate of 61.4%. The presence of additional anatomical anomalies was the only predictor of mortality among liveborn infants.

Résumé

Objectif : Résumer les issues cliniques des cas de hernie diaphragmatique congénitale (HDC) identifiés dans le cadre de l'échographie prénatale.

Méthode : Nous avons analysé les cas diagnostiqués (entre juillet 2000 et septembre 2009, au sein d'un même établissement de soins tertiaires) de HDC détectés pendant la période prénatale.

Résultats : Nous avons identifié 91 cas. Nous disposions de dossiers médicaux complets (y compris le caryotype) dans 69 de ces cas. Parmi ceux-ci, 40 constituaient des anomalies isolées et 29 présentaient des anomalies congénitales ou chromosomiques additionnelles. De façon globale, un caryotype anormal était présent dans 17,4 % des cas, affectant 2,5 % des cas de HDC isolée (1/40) et 37,9 % des cas de HDC non isolée (11/29). Le taux d'interruption de grossesse a été de 33,3 % (10/30), dans les cas de HDC isolée diagnostiqués avant 24 semaines, et de 73,9 % (17/23), dans les cas de HDC non isolée. Chez les 44 enfants nés vivants, le taux de survie a été de 66,7 % (24/36), pour ceux qui présentaient une HDC isolée, et de 37,5 % (3/8), pour ceux qui présentaient une HDC non isolée. La décision d'interrompre la grossesse a été prise dans 73,9 % des cas de fœtus dont le caryotype avait été établi ou dont les anomalies anatomiques additionnelles avaient été diagnostiquées pendant la période prénatale, par comparaison avec 37,5 % des cas de HDC isolée ayant été diagnostiqués pendant la période prénatale.

Conclusion : Les issues des grossesses qui se poursuivent à la suite de l'identification de la HDC correspondent à ce qui a été signalé auparavant, le taux global de survie étant de 61,4 %. La présence d'anomalies anatomiques additionnelles était le seul facteur prédictif de mortalité chez les enfants nés vivants.

Key Words: CDH, congenital diaphragmatic hernia, fetal malformation, outcome, pregnancy

Competing interests: None declared.

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INTRODUCTION

Congenital diaphragmatic hernia (CDH), with an incidence of 1 in 2500 to 1 in 5000 live births,[1-4] is an anatomical defect that occurs when prenatal closure of the pleural membrane is delayed, resulting in an opening between the thoracic and abdominal cavities.[1,2] Depending on the size and location of this opening, various abdominal organs can be displaced into the thoracic cavity, compressing the developing lungs and leading to pulmonary hypoplasia.[2,5] CDH can be surgically corrected, but it is often associated with high perinatal mortality and morbidity.[5] The survival of infants

with CDH depends on the degree of associated pulmonary hypoplasia and the presence of other anomalies, which can be categorized into two broad groups: anatomical and chromosomal. Further, infants with CDH and additional anatomical anomalies are more likely to have chromosomal abnormalities.[6] Although prenatal in utero interventions are being studied in clinical trials at multiple international centres,[7] this therapy is not routinely available in our centre.

Outcome review studies of prenatally diagnosed cases of CDH in the United Kingdom and Australia have shown survival rates of live-born infants after repair to discharge of 72.6% and 74% respectively.[6,8] Our study describes the conduct of pregnancy and outcome in prenatally diagnosed cases of CDH identified within a nine-year period at the British Columbia Women's Hospital, the tertiary care centre for the province of British Columbia (BC). A retrospective review of our case series was carried out to determine pregnancy outcomes when CDH was diagnosed prenatally. The data were used to compare Canadian outcomes with those of other centres over a comparable time period.

METHODS

We reviewed maternal and infant medical records of suspected CDH identified prenatally between July 2000 and September 2009 at BC Women's Hospital. We excluded cases in which CDH was first diagnosed either at birth or at autopsy. We collected demographic data (age, ethnicity, marital status, education level, home community within the province, family and pregnancy histories), prenatal screening and diagnostic results (maternal serum screening, amniocentesis, ultrasound and MRI findings), pregnancy outcomes (live birth, intrauterine fetal demise, pregnancy termination) and confirmation of CDH by autopsy or postnatal examination. In addition, factors that have been associated with poor outcome were reviewed: abdominal circumference less than the 10th centile, lung to head ratio less than 1.0, other associated congenital anomalies, liver herniation, and aneuploidy.[5] Microarray data were not available because the case series preceded the routine use of prenatal chromosome microarray at our centre.

Continuous data were summarized using median, interquartile range, and minimum and maximum values. Categorical data were summarized by univariate and joint frequency distributions. A two-tailed Fisher exact test was then used to analyze the categorical data. Statistical analyses of continuous and categorical data were performed using the descriptive statistics function in Microsoft Excel 2003 (Microsoft Corp., Redmond, WA) and SABER (Statistical Analysis Battery for Epidemiological Research) version 1.96, respectively. P-values <0.05 were considered significant.

The Research Ethics Boards at University of British Columbia and the British Columbia Children's and Women's Hospital Review Committee approved this study.

RESULTS

Ninety-one cases of prenatally diagnosed suspected CDH were identified in this study. In four cases, complete medical evaluations were not available. CDH was confirmed in 75 cases and ruled out in 12. In the cases in which CDH was ruled out, one had isolated diaphragmatic eventration, four had diaphragmatic eventration with other anatomical defects and abnormal karyotype, two had a significant heart defect, one had congenital pulmonary airway malformation, one had gastroschisis, one had multiple congenital anomalies, and two had no defects identified at birth or autopsy.

Of the 75 cases in which otherwise complete records were available, six did not have karyotyping performed. All six cases presented as isolated CDH. The remaining 69 cases had complete prenatal ultrasound and karyotyping data. Of these 69 cases, two were unusual. One case of isolated CDH had normal results on FISH for aneuploidy, but a full karyotype was not available because of failed culture after amniocentesis. One case of non-isolated CDH had normal FISH results for aneuploidy but full karyotyping showed mosaicism for monosomy X (2 cells with monosomy X and 12 cells with a 46, XX karyotype). Postnatal karyotyping was not done in either case. All 75 confirmed cases of CDH were analyzed for this study where possible. The categories of included and excluded cases are summarized in Figure.

The average maternal age in these cases was 29.5 years. In the majority of cases, the mother was Caucasian (46/75) and located in the Vancouver metropolitan area (43/75), with a travel time to BC Women's Hospital of up to one hour. The prenatal diagnosis of CDH was made at a median gestational age of 20+0 weeks, and women were assessed at a median gestational age of 21+5 weeks. When stratified based on location, women who lived in the Vancouver metropolitan area tended to have the diagnosis made nine gestational days earlier than those who did not. In addition, they accessed BC Women's Hospital services one week and four days after diagnosis, an average of two weeks earlier than women who lived outside the Vancouver metropolitan area. The tertiary level care provided additional information as appropriate, including level 3 ultrasound scans, magnetic resonance imaging (MRI), and consultations with specialists in medical genetics,